AMENDMENTS TO THE SPECIFICATION:

Please amend the specification as follows:

Please delete the paragraph at page 1, lines 9-31, of the specification and insert the following replacement paragraph:

A deterioration of neuronal cytoskeleton is observed in the majority of CNS lesions and neurodegenerative diseases. This deterioration can be the consequence but also the cause of damage to the affected cells. Indeed, microtubule depolymerization can be directly responsible for the dysfunction of certain neurons and can result in their death. Moreover, this deterioration affects the number and the length of the neuritic extensions of the remaining neuronal cells and, as a consequence, decreases their effectiveness. Treatment with NGF, which prevents dendritic atrophy, enables better functional recovery after a lesion of the cerebral cortex in the rat (Kolb et al., Neuroscience 1996). The degradation of the cytoskeleton observed after trauma to the CNS (Zhang et al., J Neuropathol Exp Neurol 2000) or an episode of ischemia, results from many factors, in particular the increase in glutamate and intracellular Ca^{++}, which involves microtubule depolymerization, and in the activation of proteases such as calpain which degrade MPA2. The use of a calpain inhibiter (Schumacher et al., *J. Neurochem 2000*) and the salting-out of glutamate (Springer et al., *J Neurochem 1997*) make it possible to decrease the consequences of ~~medullary~~spinal cord trauma in the animal by partially preserving the cytoskeleton.

Please delete the paragraph at page 2, line 30 to page 3, line 2, of the specification and insert the following replacement paragraph:

It has been shown recently that, after cerebral ischemia, stem cells could differentiate into neurons and become integrated with the existing neuronal circuits (Nakatomi et al., *Cell 2002*). The stimulation of ~~axon~~neurite growth in these cells by molecules that improve tubulin polymerization could increase their functionality.

Please delete the paragraph at page 3, lines 11-21, of the specification and insert the following replacement paragraph:

Studies that demonstrate an effect by pregnenolone (PREG) *in vivo* are very few but they suggest a beneficial role for this steroid. It was shown that PREG decreased the astrocyte reaction following a cerebral lesion (Garcia-Estrada et al., *Int J Devl Neuroscience 1999*) and in the case of the increased astrocyte size observed during ageing (Legrand and Alonso, *Brain Res. 1998*). It also contributed to improved functional recovery after a ~~medullary~~spinal cord trauma (Guth et al., *Proc Natl Acad Sci USA 1994*). PREG protects cells arising from a hippocampal line (HT-22) against toxicity induced by glutamate and the protein beta amyloid (Gursoy et al., *Neurochem Res. 2001*).

Please delete the paragraph at page 7, lines 3-10, of the specification and insert the following replacement paragraph:

In a preferred embodiment according to the invention, the aforementioned disease is selected from the group comprising Alzheimer's disease, Parkinson's disease, age-induced memory loss, memory loss induced by the taking of substances, a traumatic lesion, a cerebral lesion, a lesion of the spinal cord, in particular ~~medullary~~spinal cord compression, ischemia, pain, notably ~~neuritic pain~~neuralgia, nerve degeneration, and multiple sclerosis.

Please delete the paragraph at page 7, lines 22-27, of the specification and insert the following replacement paragraph:

The pharmaceutical compositions used in the invention can be administered by any route of administration including, but not being limited to, oral, intravenous, intramuscular, intraarterial, ~~intramedullary~~intraspinal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, and rectal.

Please delete the paragraph at page 12, lines 20-25, of the specification and insert the following replacement paragraph:

The invention also relates to a method for increasing the growth of ~~axons~~neurites in a cell, comprising the step of exposing the aforementioned cell to the presence of 3-methoxy-PREG at a concentration from approximately 0.5 to 50 µM. This method is also recommended *in vitro* by preference, without excluding other modes of implementation if necessary.

Please delete the paragraph at page 17, lines 26-32, of the specification and insert the following replacement paragraph:

The invention has also as an aim a method for reducing the depolymerization of microtubules and/or the retraction of ~~axon~~neurites in a cell, comprising the step of exposing the aforementioned cell to the presence of 3-methoxy-PREG at a concentration from approximately 0.5 to 50 µM. This method is implemented *in vitro* also by preference, without excluding other modes of implementation if necessary.

Please delete the paragraph at page 13, lines 10-14, of the specification and insert the following replacement paragraph:

Finally, a method to treat a patient after ~~medullary~~ spinal cord compression or trauma, comprising the step of the administration of an effective quantity of 3-methoxy-PREG to the aforementioned patient, is also an object of the invention.

Please delete the paragraph at page 13, line 28 to page 14, line 2 of the specification and insert the following replacement paragraph:

Figure 2: Effect of PREG and 3-methoxy-PREG (43B) on the average length of ~~axons~~neurites in PC12 cells. PC12 cells were cultured for 3 days in the presence of NGF (10 ng/ml) with or without (control) the addition of PREG or 43B molecules (30 μM). Each molecule was tested in three culture wells. Measurements were taken for 200 cells per well using Scion Image software.

Please delete the paragraph at page 14, lines 3-8, of the specification and insert the following replacement paragraph:

Figure 3: Dose-response relationship of molecule 43B on the average length of ~~axons~~neurites in PC12 cells. PC12 cells were cultured in the presence of NGF (10 ng/ml) and increasing concentrations of 3-methoxy-PREG (43B). ~~Axon~~Neurite length was measured for 200 cells per well after 2, 5, and 8 days of culture.

Please delete the paragraph at page 14, lines 9-14, of the specification and insert the following replacement paragraph:

Figure 4: Immunolabeling of microtubule-associated MAP2 in PC12 cells treated with PREG or 3-methoxy-PREG. PC12 cells were cultured in the presence of NGF (10 ng/ml) and PREG or 3-methoxy-PREG (20 μM). They are fixed and exposed to anti-MAP2 antibodies that reveal microtubule-associated MAP2 exclusively.

Please delete the paragraph at page 14, lines 15-19, of the specification and insert the following replacement paragraph:

Figure 5: Retraction of ~~axons~~neurites induced by nocodazole. After 7 days of culture in the presence of NGF (10 ng/ml), the cells were pretreated for one hour with PREG (30 µM) or 43B (30 µM), then exposed to nocodazole for 15 minutes (white columns: DMSO solvent alone; gray columns: nocodazole).

Please delete the paragraph at page 14, lines 26-32, and insert the following replacement paragraph:

Figure 7: Effect of molecule 43B on locomotor recovery following ~~medullary~~ spinal cord compression in rats. Animal locomotion was evaluated in a blind format during the 1-28 day post-operative period using the BBB score which evaluates the degree of paralysis (higher values correspond to better recovery). Statistical significance: * indicates $p < 0.001$; ** indicates $p < 0.0001$.

Please delete the paragraph at page 16, lines 22-23, of the specification and insert the following replacement paragraph:

Example 3: Cellular models

Effect of molecules on ~~neurites' growth~~neurite outgrowth

Please delete the paragraph at page 16, line 16, line 24 to page 17, line 8, of the specification and insert the following replacement paragraph:

To test the effect of selected molecules on ~~neurites' growth~~neurite outgrowth, we first used the PC12 lines, which has long been employed in neurobiological research. In the presence of NGF (nerve growth factor), the cells of this line, which arise from a rat pheochromocytoma, form neuritic extensions containing MAP-associated

microtubules. The growth of these elongations is stimulated by the addition of PREG. In the presence of PREG (30μM), the increase in the average length of the ~~axons~~neurites after 4 days of culture reaches 60%. The screening of other natural or synthetic steroids made it possible to select several molecules presenting greater effects than that of PREG (Figure 2). In particular, the addition of molecule 43B, which can be synthesized easily from PREG, caused a spectacular increase (reaching as high as 500%) in the length of ~~axons~~neurites formed in the presence of NGF (Figure 3). This ~~axon~~neurite growth accompanies the estimation by 43-B of the association of MAP to the microtubules (Figure 4).

Please delete the paragraph at page 17, lines 12-19, of the specification and insert the following replacement paragraph:

Nocodazole is a microtubule depolymerizing agent. Its addition to PC12 cell cultures, differentiated in the presence of NGF, causes ~~axons~~neurites to retract as a result of the depolymerization of their microtubules. Pretreatment of the cells by PREG or 43B makes the ~~axons~~neurites resistant to nocodazole due to an increase in the stability of their microtubules, a condition necessary for the formation of long ~~axons~~neurites (Figure 5).

Please delete the paragraph at page 18, lines 6-8, of the specification and insert the following replacement paragraph:

In rats, the daily injection for one month of 48 mg/kg of 43B (which is 4 times the active dose for ~~medullary~~spinal cord trauma) affected neither average weight nor behavior.

Please delete the paragraph at page 18, lines 10-21, of the specification and insert the following replacement paragraph:

Example 5: In vivo experiments - ~~Medullary~~ spinal cord trauma

~~Medullary~~ spinal cord contusion model

To determine the neuroprotective effects of the molecules tested, a ~~medullary~~ spinal cord compression model is used. This model involves the total paralysis of the animals in the first few days following the operation. This period of paralysis is followed of a phase of approximately three weeks during which the animals partially recover their motor function. The study of this recovery using a simple and precise functional test based on observation of the animals (the BBB score) makes it possible to study the speed and the degree of recovery of the animals, with and without treatment.

Please delete the paragraph at page 18, line 22 through page 19, line 2, of the specification and insert the following replacement paragraph:

Two groups of rats were subjected to ~~medullary~~ spinal cord compression. Then, daily for 2 weeks, the animals received a subcutaneous injection containing either sesame oil alone (control group, n=20), or sesame oil containing molecule 43B (43B group, n=20; 12 mg/kg/day). The first injection was given 5 minutes after ~~medullary~~ spinal cord compression. Locomotion of the animals, using BBB scores, was evaluated in a blind format on post-operation days 1, 4, 7, 14, 21, and 28. Three animals in each group had to be excluded from the study. Statistical analysis of the results using the nonparametric Mann-Whitney test shows that the animals treated with 43B present results quite significantly higher than the control animals as of post-operation day 7 (Figure 7).

Please delete the paragraph at page 19, lines 23-31, of the specification and insert the following replacement paragraph:

These mice express the longest human tau protein isoform. They present symptoms of neurological dysfunction expressed as muscular weakness and a reduction in motor coordination which correlate histologically with the appearance of abnormal ~~axons~~neurites and hyperphosphorylated tau proteins as is seen in Alzheimer's disease. This pathological phosphorylation decreases the affinity of tau for microtubules and favors its aggregation.

Please delete the paragraph at page 21, lines 18-21, of the specification and insert the following replacement paragraph:

These results obtained *in vitro* and *in vivo* clearly demonstrate that molecule 43B (3-methoxy-PREG) gives spectacular results on the growth of ~~axons~~neurites in culture and on the ~~medullary~~spinal cord compression model.

Please delete the paragraph at page 21, lines 24-25, of the specification and insert the following replacement paragraph:

Example 10: Other molecules according to the invention

The indices of ~~bonding~~ binding and activity are expressed as a percent of PREG.

Please delete the paragraph at page 21, lines 26-27, of the specification and insert the following replacement paragraph:

Bionding (affinity) is measured by the displacement of PREG-^{3}H.

Please delete the paragraph at page 21, line 31 to page 22, line 2, of the specification and insert the following replacement paragraph:

Stimulation of ~~neuritic neurites' sprouting~~neurite outgrowth is conducted on PC12 cells differentiated in the presence of NGF (10 ng/ml) and the steroid being tested (30 µM) for 3 days. For each condition, the average length of the longest 200 ~~axon~~neurites in each cell is measured simultaneously for 3 cultures.

Please delete the paragraph and the embedded Table at page 22, lines 3-7, of the specification and insert the following replacement paragraph and Table:

The results are represented by one, two or three crosses (+) according to whether stimulation is lower than, equal to, or higher than that produced by PREG.

Steroid	***Affinity***	***Activity***	***~~Neuritic~~ Neurite sprouting***
Pregnenolone (PREG)	100	100	++
3β-methoxy-pregna-5-ene-20-one	100	100	+++
3β-methoxy-pregna-5-ene-20-one-17α-dichloromethyl	53	113	+++
3β-methoxy-5α- pregnane-20-one	87	10	+++
3β-methoxy-5α-pregnane-20β-ol	65	65	++
PREG-16α-methyl	80	70	++
PREG-16β-methyl	63	67	(++)
3β-methoxy-pregna-5,14-diene-20-one	102	50	+
PREG-16α,17α-epoxy	41	54	+
PREG-16α,17α-methylene	62	49	+
Pregna-5-ene-3β,20β-diol-20-acetate	60	108	++
3β-hydroxy-5α-pregnane-20-one-16α-methyl	57	53	(+)

Please delete the paragraph at page 22, lines 8-13, of the specification and insert the following replacement paragraph:

These results show the effectiveness of other molecules derived from pregnenolone to stimulate the polymerization of microtubules induced by MAP2 and to stimulate ~~neuritic~~ neurite sprouting. For those that are not 3β-methyl derivatives, it is foreseeable that these derivatives will at least maintain their activity.